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UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

VANDA PHARMACEUTICALS INC., Plaintiff, v. TEVA PHARMACEUTICALS USA, INC., Defendant.	Civil Action No. 22-7528-CCC
VANDA PHARMACEUTICALS INC., Plaintiff, v. APOTEX INC. and APOTEX CORP., Defendants.	Civil Action No. 22-7529-CCC *Document Electronically Filed* **ORAL ARGUMENT REQUESTED**

MEMORANDUM IN SUPPORT OF PLAINTIFF'S MOTION FOR TEMPORARY RESTRAINING ORDER*

* Vanda is filing this identical memorandum of law in support of its motion for a temporary restraining order in each of the above-captioned cases.

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INTRODUCTION

This is a request for a temporary restraining order, pursuant to Federal Rule of Civil Procedure 65, to preserve the status quo for a brief period of time in the face of extraordinary circumstances. Plaintiff Vanda Pharmaceuticals Inc. (Vanda) is a small pharmaceutical company with the first and only FDA-approved therapy—Hetlioz® (tasimelteon)—to treat two debilitating and rare conditions. Hetlioz® is extraordinarily important to Vanda: Vanda has only two principal products in the market, and Hetlioz® accounted for approximately 65% of Vanda's revenue in 2021.

Defendants Teva Pharmaceuticals USA, Inc. (Teva) and Apotex Inc. and Apotex Corp. (Apotex) are on the precipice of each launching a generic version of tasimelteon, with Teva telling the Federal Circuit in the last two weeks that it has "FDA final approval and the ability to immediately launch a generic tasimelteon product."[1] Teva is a pharmaceutical giant, with approximately 500 approved products in the market, and revenues of approximately $16 billion USD. Apotex

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[1] *See* Teva Pharmaceuticals USA, Inc.'s Non-Confidential Emergency Mot. for Review, Reconsideration, or Modification of Temporary Injunction at 2, *Vanda Pharms. Inc. v. Teva Pharms. USA, Inc.*, No. 23-1247 (Fed. Cir. Dec. 19, 2022), ECF No. 9.

Apotex has similarly represented its intent to imminently launch. *See* Apotex's Opp. to Appellee Teva's Emergency Mot. at 1, *Vanda Pharms. Inc. v. Teva Pharms. USA, Inc.*, No. 23-1247 (Fed. Cir. Dec. 21, 2022), ECF No. 16; Appellees' Response in Opp. to Appellant's Rule 8 Mot. for an Injunction Pending Appeal at 14, *Vanda Pharms. Inc. v. Teva Pharms. USA, Inc.*, No. 23-1247 (Fed. Cir. Dec. 23, 2022), ECF No. 25.

similarly has roughly 300 products, and revenues of approximately $2 billion USD.

Teva and Apotex were barred from launching their generics until yesterday afternoon: Although they had prevailed in earlier patent litigation with Vanda before the district court, the Federal Circuit had issued a temporary injunction precluding Teva and Apotex from launching. However, yesterday afternoon, December 28, 2022, the Federal Circuit lifted that stay. Now, nothing bars Teva and Apotex from launching—save a temporary restraining order from this Court.

In this lawsuit, Vanda will show that Teva's and Apotex's generic product will infringe (or induce infringement) of a recently-issued patent owned by Vanda, U.S. Patent No. 11,285,129 (the '129 patent). This patent is entirely unrelated to Vanda's earlier litigation between with Teva and Apotex—indeed, the patent issued *mid-trial*, and had nothing to do with that case. Teva and Apotex did not send Hatch-Waxman Paragraph IV letters regarding this patent until September and June 2022 respectively.

Presently, Vanda asks the Court to issue a temporary restraining order to preserve the status quo for a limited period of time solely to allow this Court to adjudicate a fully-briefed motion for a preliminary injunction. Such relief is warranted under the circumstances.

First, the harm to Vanda should Teva and Apotex not be enjoined is irreparable: If Teva and Apotex launch generic products, it would inflict enormous,

irreparable damage on Vanda. Because Hetlioz® represented roughly 65% of Vanda's revenue in 2021, the injuries to the company would be dire. Not only does a generic launch risk Vanda's financial ruin, but further irreparable injuries abound—Vanda would lose critical revenue necessary for its several, significant research programs, as it reinvests more than 90% of its revenues into research and development and operations; Vanda may be forced to lay off irreplaceable staff; and the market for tasimelteon would forever erode.

Second, Vanda has a great likelihood of success. While Teva and Apotex will no doubt point to their earlier litigation victory over Vanda, that has simply nothing to do with the '129 patent at issue here. The '129 patent covers Vanda's novel innovations regarding the co-administration of tasimelteon with beta-adrenergic blocking agents (better known as beta blockers). More specifically, the '129 patent describes the unexpected finding that tasimelteon and a beta blocker should *not* be administered together because of a previously unknown drug interaction. Thus, Vanda invented a new way of administering tasimelteon that reflects the previously unknown interaction problem with beta blockers. By submitting prescribing information with their ANDAs that encourages physicians to counsel their patients not to take beta blockers with tasimelteon, Teva and Apotex have infringed the '129 patent. And because (if allowed to enter the market) Teva and Apotex will sell product with instructions that doctors would interpret as warning against the co-

administration of beta blockers and tasimelteon, Teva and Apotex are steps away from infringing the '129 patent again.

Third, the equities and public interest overwhelmingly favor temporary relief. This is a David versus Goliath situation: While Vanda faces devastating consequences to its business, Teva and Apotex stand to lose money. For both Teva and Apotex, the amount of money at stake here is trivial—amounting to a fraction of a percent of each company's total annual revenue. In any event, Vanda will post a significant bond more than sufficient to compensate Teva and Apotex for any harm they may later demonstrate on account of being improperly temporarily enjoined.

BACKGROUND

A. Vanda and its Hetlioz® product

Vanda is a small pharmaceutical company that focuses on the development and commercialization of new medicines to address unmet medical needs. Teva Verified Compl. ("TVC") ¶ 20; Apotex Verified Compl. ("AVC") ¶ 24. It acquires compounds that failed in development by other drug companies and turns them into successful FDA-approved therapies. TVC ¶ 20; AVC ¶ 24. Vanda only has two FDA-approved products: the product at issue in this case, Hetlioz® (tasimelteon), which accounted for nearly 65% of Vanda's 2021 revenue, and Fanapt® (iloperidone). Moran Decl. ¶¶ 4, 7.

Vanda purchased tasimelteon from a large pharmaceutical company that had

tried and failed to develop the molecule into a useful FDA-approvable therapy. TVC ¶ 21; AVC ¶ 25. Through hard work and ingenuity, Vanda's investment paid off when it showed that 20 mg of tasimelteon, taken once-daily before a target bedtime, can treat a debilitating condition that principally affects totally blind people called Non-24-Hour Sleep-Wake Disorder ("Non-24"). TVC ¶¶ 22, 25-26; AVC ¶¶ 26, 29-30. Tasimelteon thus became Hetlioz®, the first and only FDA-approved treatment for Non-24. TVC ¶¶ 22-23; AVC ¶¶ 26-27. Following additional research and development by Vanda, on December 1, 2020, the FDA approved Hetlioz for the additional indication of treating nighttime sleep disturbances in the rare debilitating disorder Smith-Magenis Syndrome. TVC ¶ 23; AVC ¶ 27.

Vanda's trailblazing work also led to several patents, including the patent asserted in this case, the '129 patent. TVC Ex. A; AVC Ex. A.

B. The '129 Patent

Stemming from a 2012 provisional application, on March 29, 2022, the '129 patent issued, claiming a method of administering tasimelteon to a patient without beta-adrenergic antagonists (*i.e.*, beta blockers). The '129 patent specifically claims:

> 1. In a method of administering tasimelteon to a patient, the improvement comprising:
>
> determining whether the patient is being treated with a
>
> beta-adrenergic receptor antagonist; and
>
> in the case that it is determined that the patient is not being treated with a beta-adrenergic receptor antagonist, administering to the

> patient 20 mg of tasimelteon once daily about one-half hour to about one-and-one-half hours before the target bedtime;
>
> or
>
> in the case that it is determined that the patient is being treated with a beta-adrenergic receptor antagonist:
>
> instructing the patient to cease treatment with the beta-adrenergic receptor antagonist; and then administering to the patient 20 mg of tasimelteon once daily about one-half hour to about one-and-one-half hours before the target bedtime.

TVC Ex. A at 38:41-56; AVC Ex. A at 38:41-56.

Claim 2 limits the improvement to specific beta-blockers, and claim 3 further limits the improvement as applied to methods of administering tasimelteon for patients with Non-24. TVC Ex. A at 38:41-56; AVC Ex. A at 38:41-56.

C. Field of the Invention

As mentioned above, Non-24 is a rare orphan disorder that disproportionately affects those who are completely blind. *See* TVC Ex. A at 1:62-67; AVC Ex. A at 1:62-67. "[U]nable to synchronize their endogenous circadian pacemaker to the 24-hour light/dark cycle," "[i]ndividuals with Non-24 have abnormal night sleep patterns, accompanied by difficulty staying awake during the day." TVC Ex. A at 2:1-8; AVC Ex. A at 2:1-8. "Non-24 leads to significant impairment, with chronic effects impacting the social and occupational functioning of these individuals." TVC Ex. A at 2:8-10; AVC Ex. A at 2:8-10.

In 2014, Vanda received FDA approval for Hetlioz. Tasimelteon, the active

ingredient in Hetlioz®, "is a melatonin agonist that has been demonstrated, among other activities, to entrain patients suffering from Non-24." TVC Ex. A at 4:32-35; AVC Ex. A at 4:32-35.

In its work to develop Hetlioz®, Vanda sought to understand why certain patients might not to respond to tasimelteon. One of those factors, Vanda discovered, was co-administration of tasimelteon with "beta-adrenergic receptor antagonists, commonly referred to as 'beta blockers,'" which are "commonly prescribed" drugs used to treat, among other things, numerous heart conditions. *See* TVC Ex. A at 8:65-67-9:1-4; AVC Ex. A at 8:65-67-9:1-4.

Scientific literature had suggested, before the priority date of the '129 patent, that beta blockers could be useful in the treatment of circadian rhythm disorders. *E.g.*, Weisbruch Decl. Ex. 11 (Leersnyder 2001) at 586. But through Vanda's experimental research designed to understand the effects of tasimelteon, the '129 patent inventors determined that "patients receiving beta blocker therapy were *less likely* to become entrained than patients who were not." TVC Ex. A at 24:63-67, Table 4 (emphasis added); AVC Ex. A at 24:63-67, Table 4 (emphasis added). Indeed, in a clinical study described in the specification of the '129 patent, 55% of patients without beta blockers were entrained versus 0% of people on beta blockers. *Id.* at Table 4; *see also* TVC Ex. A, Tables 3A, 3B; AVC Ex. A, Tables 3A, 3B (patients with higher endogenous urinary melatonin showed vastly different success

rates (85% entrainment) as compared to those with much less urinary melatonin (38%)). In other words, Vanda unexpectedly determined that co-administration of beta blockers—a widely prescribed class of medication—and tasimelteon led to decreased efficacy of tasimelteon in patients with Non-24. The '129 patent claims a method of administering tasimelteon to a patient, the method comprising, *inter alia*, "determining whether the patient is being treated with a [beta blocker]" and, if so, "instructing the patient to cease treatment with the [beta blocker]" and "administering 20 mg of tasimelteon" at the claimed dosage and time. TVC Ex. A at 38:41-56; AVC Ex. A at 38:41-56.

Tellingly, long after Hetlioz has been approved and on the market, scientific literature continued to suggest that co-administration of beta blockers with melatonin could demonstrate patient benefits in circadian rhythm disorders. Weisbruch Decl. Ex. 12 (Gehrman 2021) at 2121-23 (discussing the use of a combination of a beta blocker and the administration of exogenous melatonin in treating a patient with a circadian rhythm disorder).

D. Teva's ANDA and its to-be-marketed generic

On September 12, 2022, Teva notified Vanda that it submitted a Paragraph IV certification for the '129 patent for its tasimelteon ANDA No. 211601. Weisbruch

Decl. Ex. 1 (Teva's Paragraph IV Certification).[2] Teva's Paragraph IV certification states that the "active ingredient in the proposed drug is Tasimelteon; the strength of the proposed drug product in Teva's ANDA is 20 mg; and the dosage form of the proposed drug product is a capsule." *Id.* at 2. Under bedrock FDA law, Teva attached (as required) what it purported to be a "a detailed statement of the factual and legal basis of the opinion of the applicant that the patent is invalid or will not be infringed." 21 U.S.C. § 355(b)(3)(D)(ii); Weisbruch Decl. Ex. 1 (Teva's Paragraph IV Certification) app. Teva did not include any developed argument alleging that the '129 patent was invalid; rather, it made only claims of non-infringement. Weisbruch Decl. Ex. 1 (Teva's Paragraph IV Certification) app. at 7-8.[3]

As part of its ANDA submission, Teva included prescribing information that would be packaged along with the tasimelteon product it intends to sell. In relevant part, Teva's proposed label says that "[t]asimelteon capsules are indicated for the treatment of Non-24 in adults" with a "recommended dosage of … 20 mg one hour before bedtime, at the same time every night." Weisbruch Decl. Ex. 2 (Teva's Label)

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[2] A Paragraph IV certification by an ANDA applicant is a representation that "in [the applicant's] opinion … and to the best of its knowledge, ... the [certified] patent is invalid, unenforceable, or will not be infringed by the manufacture, use, or sale of the drug product for which the ANDA is submitted." 21 C.F.R. § 314.94(a)(12)(i)(A)(4); *see also* 21 U.S.C. § 355(b)(2)(A)(iv).

[3] Teva merely reserved its rights in a conclusion to "develop and make other arguments," like those made in prior litigation or on obviousness grounds. Weisbruch Decl. Ex. 1 (Teva Paragraph IV Certification) at 8.

at 2. It further explains that tasimelteon is a melatonin receptor agonist at two receptors "which are thought to be involved in the control of circadian rhythms." *Id.* at 5. In the section on drug interactions, Teva's prescribing information explains that "[b]eta-adrenergic receptor antagonists have been shown to reduce the production of melatonin via specific inhibition of beta-1 adrenergic receptors. Nighttime administration of beta-adrenergic receptor antagonists may reduce the efficacy of tasimelteon." *Id.* at 3.

Based on the label that Teva proposed and the statutory obligation for an ANDA applicant to use the same labeling (21 U.S.C. § 355(j)(2)(A)(v)), Vanda believes that Teva's prescribing information will be included with the product it imminently intends to sell. TVC ¶ 38.

E. Apotex's ANDA and its to-be-marketed generic

On June 15, 2022, Apotex notified Vanda that it submitted a Paragraph IV certification for the '129 patent for its tasimelteon ANDA No. 211607. Weisbruch Decl. Ex. 3 (Apotex's Paragraph IV Certification) at 1-2. Apotex's Paragraph IV certification states that the "active ingredient in the proposed drug product is tasimelteon; the strength of the proposed drug product is 20 mg; and the dosage form of the proposed drug product is a capsule." *Id.* at 2. Apotex attached (as required) what it purported to be a "a detailed statement of the factual and legal basis of the opinion of the applicant that the patent is invalid or will not be infringed." 21 U.S.C.

§ 355(b)(3)(D)(ii); Weisbruch Decl. Ex. 3 (Apotex's Paragraph IV Certification). Apotex did not include any argument about how the '129 patent was invalid; it only provided arguments asserting non-infringement. Weisbruch Decl. Ex. 3 (Apotex's Paragraph IV Certification) at A-25-26.

As part of its ANDA submission, Apotex included prescribing information that would be packaged along with the tasimelteon product it intends to sell. In relevant part, Apotex's proposed label says that "[t]asimelteon capsules are indicated for the treatment of Non-24 in adults" with a "recommended dosage" of "20 mg one hour before bedtime, at the same time every night." Weisbruch Decl. Ex. 4 (Apotex's Label) at 3. It further explains that tasimelteon is a melatonin receptor agonist at two receptors "which are thought to be involved in the control of circadian rhythms." *Id.* at 7. In the section on drug interactions, Apotex's prescribing information explains that "[b]eta-adrenergic receptor antagonists have been shown to shown to reduce the production of melatonin via specific inhibition of beta-1 adrenergic receptors. Nighttime administration of beta-adrenergic receptor antagonists may reduce the efficacy of tasimelteon." *Id.* at 4.

Based on the label that Apotex proposed and the statutory obligation for an ANDA applicant to use the "same labeling" (21 U.S.C. § 355(j)(2)(A)(v)), Vanda believes that Apotex's prescribing information will be included with the product it imminently intends to sell. AVC ¶ 42.

F. Procedural History

1. Prior litigation

Teva and Apotex originally filed their ANDAs with FDA on January 31, 2018, each seeking approval for the commercial manufacture, use, and sale of a generic version of Vanda's Hetlioz product. *See* Weisbruch Decl. Ex. 5 (Teva's ANDA Tentative Approval) at 1; Ex. 6 (Apotex's ANDA Tentative Approval) at 1. As required by the Hatch-Waxman Act, Teva and Apotex each sent a notice letter to Vanda explaining why the patents then listed in the Orange Book were either not infringed or invalid. Opinion ¶¶ 37-39, 41-42, *Vanda Pharms. Inc. v. Teva Pharms. USA, Inc.*, No. 18-cv-651 (D. Del. Dec. 13, 2022), ECF No. 336. Vanda sued in the normal course. As additional patents issued during the course of the litigation, Vanda listed them, Teva and Apotex sent notice letters to Vanda, and several patents were added to the litigation. *See, e.g.*, Stipulation to Amend Compl., *Vanda Pharms. Inc. v. Teva Pharms. USA, Inc.*, No. 18-cv-651 (D. Del. Dec. 7, 2018), ECF No. 38. Ultimately, through forced narrowing of the asserted patents and claims by the district court, Vanda limited its assertions to just one claim each of four patents. *See* Final Judgment, *Vanda Pharms. Inc. v. Teva Pharms. USA, Inc.*, No. 18-cv-651 (D. Del. Dec. 13, 2022), ECF No. 338.

FDA approved Teva's tasimelteon ANDA product on December 12, 2022. Weisbruch Decl. Ex. 7 (Teva's ANDA Final Approval). The next day, the district

court found in favor of Teva and against Vanda. Opinion at 71, *Vanda Pharms. Inc. v. Teva Pharms. USA, Inc.*, No. 18-651-CFC (D. Del. Dec. 13, 2022), ECF No. 336. Vanda promptly appealed. In the meantime, FDA approved Apotex's ANDA product on December 20, 2022. Weisbruch Decl. Ex. 8 (Apotex's ANDA Final Approval).

The Federal Circuit temporarily enjoined Teva and Apotex from commercial marketing and sale of their tasimelteon ANDA product until the Court could rule on Vanda's motion whether to enter an injunction pending appeal. Order on Motion for Injunction Pending Appeal, *Vanda Pharms. Inc. v. Teva Pharms. USA, Inc.*, No. 23-1247 (Fed. Cir. Dec. 16, 2022), ECF No. 6; Order on Motion to Lift Temporary Injunction, *Vanda Pharms. Inc. v. Teva Pharms. USA, Inc.*, No. 23-1247 (Fed. Cir. Dec. 22, 2022), ECF No. 23. Ultimately, on December 28, 2022, the Federal Circuit expedited Vanda's appeal of the district court's decision on Vanda's four other patents but denied Vanda's request for an injunction pending that appeal without providing any reasoning. *See* Order, *Vanda Pharms. Inc. v. Teva Pharms. USA, Inc.*, No. 23-1247 (Fed. Cir. Dec. 28, 2022), ECF No. 27.

2. The operative complaint

In the midst of the four-day bench trial in the pre-approval Hatch-Waxman litigation, the '129 patent issued. TVC Ex. A; AVC Ex. A. Because trial was underway, there was no opportunity to litigate infringement of the '129 patent and

address the new and novel issues it raised. TVC ¶ 41; AVC ¶ 45.

Vanda thus filed these actions on December 27, 2022, to assert the '129 patent, and it now seeks a temporary restraining order to maintain the status quo to prevent Teva's and Apotex's launch of generic tasimelteon products, until such time as this Court may adjudicate Vanda's forthcoming motion for a preliminary injunction.

ARGUMENT

The Court should enter a temporary restraining order that preserves the status quo—that is, that precludes Teva and Apotex from launching—until such time as the Court can adjudicate an orderly motion for a preliminary injunction. Doing so is necessary to preserve this Court's ability to fashion relief, if it later determines that a preliminary injunction is warranted. By contrast, if the Court permits Teva and Apotex to launch now, the harms to Vanda will occur—and will forever be irreparable. Delaying Teva and Apotex from launching, however, does nothing other than cost them money. And Vanda will post a bond sufficient to cover any damages Teva and Apotex are able to later show if they were wrongly enjoined from entering the market. For these reasons, the factors of irreparable injury, the balance of equities, and the public interest all enormously favor the grant of temporary relief. Further, Vanda is likely to prevail on the merits of its claim: Teva and Apotex both infringe the '129 patent and induce others to infringe it, and defendants are unlikely to demonstrate that the patent is invalid.

When evaluating a request for a temporary injunction, this Court weighs the same four factors that it considers when evaluating a motion for preliminary injunction: (1) likelihood that the plaintiff will prevail on the merits of the claim; (2) probability the plaintiff will suffer irreparable harm if the relief is not granted; (3) balance of hardships; and (4) that granting relief will be in the public interest. *Fed'n of State Massage Therapy Boards v. Acad. of Oriental Therapy, LLC*, 2013 WL 5888094, at *1 (D.N.J. Oct. 28, 2013); *Health Pros. & Allied Emps. AFT/AFL-CIO v. MHA, LLC*, 2017 WL 6550488, at *2 (D.N.J. Dec. 21, 2017) (citing *Fres-co Sys. USA, Inc. v. Hawkins*, 690 F. App'x 72, 75 (3d Cir. 2017)). The Court must consider, "in its sound discretion if all four factors, taken together, balance in favor of granting the requested preliminary relief." *Reilly v. City of Harrisburg*, 858 F.3d 173, 179 (3d Cir. 2017); *see also Novartis Consumer Health, Inc. v. Johnson & Johnson-Merck Consumer Pharms. Co.*, 290 F.3d 578, 586 (3d Cir. 2002).

Recognizing the irreparable harm that sales of a generic competitor product can cause in the pharmaceutical market, courts in this District have repeatedly concluded that a temporary restraining order is appropriate where, like here, a generic pharmaceutical company will soon be launching a likely infringing product. *See, e.g.*, Order to Show Cause with Temporary Restraints, *Indivior Inc. v. Dr. Reddy's Labs. S.A.*, No. 17-cv-7111 (D.N.J. June 8, 2018), ECF No. 78 (granting a temporary restraining order against launch of a generic); Order for Temporary

Relief, *AstraZeneca LP v. Apotex, Inc.*, No. 09-cv-1518 (D.N.J. Apr. 21, 2009), ECF No. 45 (same). The Court should do so here too.

I. The Court should preserve the status quo by restraining Teva and Apotex from launching a generic Hetlioz® product pending preliminary injunction proceedings.

A. Vanda will likely prevail on the merits.

Vanda is likely to demonstrate that Teva and Apotex infringe the '129 patent; meanwhile, Teva and Apotex are unlikely to demonstrate that the patent is invalid.

1. Vanda will likely prove that Teva and Apotex will induce infringement of the '129 patent by the marketing and sale of its generic Hetlioz® product.

The launch of a generic product by Teva or Apotex with their product labels will induce doctors to infringe the '129 patent.[4] A person need not directly infringe—*i.e.*, make, use, offer to sell, or sell a patented invention in order to be liable for infringement; rather, "[w]hoever actively induces infringement of a patent shall [also] be liable as an infringer." 35 U.S.C. § 271(b); *see* 35 U.S.C. § 271(a) (direct infringement). Teva's and Apotex's label establishes that each induces infringement.

a. The rules for showing induced infringement based on a pharmaceutical product label are well established. The patentee must show that there is or—for purposes of pre-infringement declaratory relief—will be "direct infringement" and

[4] In demonstrating that Vanda is likely to prove that Teva and Apotex induce doctors to infringe the '129 patent via their labels, Vanda does not disclaim alternative infringement theories, which it may later advance.

that "the alleged infringer possessed the requisite intent to induce infringement," i.e., that it "knew or should have known [its] actions would induce actual infringements." *Eli Lilly & Co. v. Teva Parenteral Meds., Inc.*, 845 F.3d 1357, 1363-1364 (Fed. Cir. 2017) (citing *DSU Med. Corp. v. JMS Co.*, 471 F.3d 1293, 1304 (Fed. Cir. 2006)). Where "the proposed label instructs users to perform the patented method ... the proposed label may provide evidence of [a generic pharmaceutical company's] affirmative intent to induce infringement." *AstraZeneca LP v. Apotex, Inc.*, 633 F.3d 1042, 1060 (Fed. Cir. 2010). When proof of specific intent depends on the label accompanying the marketing of a drug inducing infringement by physicians, "[t]he label must encourage, recommend, or promote infringement." *Takeda Pharms. U.S.A., Inc. v. West-Ward Pharm. Corp.*, 785 F.3d 625, 631 (Fed. Cir. 2015). "The contents of the label itself may permit the inference of specific intent to encourage, recommend, or promote infringement." *Vanda Pharms. Inc. v. West-Ward Pharms. Int'l Ltd.*, 887 F.3d 1117, 1129 (Fed. Cir. 2018) (quoting *Sanofi v. Watson Labs. Inc.*, 875 F.3d 636, 646 (Fed. Cir. 2017)). And it is irrelevant to the inducement inquiry if "some users may ignore the warnings in the proposed label." *AstraZeneca*, 633 F.3d at 1060.

Vanda has a strong case that the prescribing information Teva and Apotex will provide will encourage doctors to infringe the claims of the '129 patent. As demonstrated in Table 1, the generic labels—which are materially identical for

relevant purposes—include language that a prescribing physician would understand to direct the infringing methods of administration of tasimelteon:

Table 1

'129 Claim 1	**Generic Label & Combs Declaration**
In a method of administering tasimelteon to a patient	Dosage and Administration section describes the recommended dosage for tasimelteon capsules and "important administration information." Weisbruch Decl. Ex. 2 (Teva's Label) at 2; Weisbruch Decl. Ex. 4 (Apotex's Label) at 3.
Determining whether the patient is being treated with a beta-adrenergic receptor antagonist	Beta-adrenergic receptor antagonists are included in the "drug interactions" section. Weisbruch Decl. Ex. 2 (Teva's Label) at 3; Weisbruch Decl. Ex. 4 (Apotex's Label) at 4. Teva's listing of beta blockers as causing a drug interaction will cause at least some physicians to determine whether their patients are taking beta blockers. Combs Decl. ¶¶ 48–53.
In the case that it is determined that the patient is not being treated with a beta-adrenergic receptor antagonist	(see above)
Administering to the patient 20 mg of tasimelteon once daily about one-half hour to about one-and-one-half hours before the target bedtime	"The recommended dosage of tasimelteon capsules in adults is 20 mg one hour before bedtime . . . ." Weisbruch Decl. Ex. 2 (Teva's Label) at 2; Weisbruch Decl. Ex. 4 (Apotex's Label) at 3.
In the case that it is determined that the patient is being treated with a beta-adrenergic receptor antagonist	(see above)

Instructing the patient to cease treatment with the beta-adrenergic receptor antagonist	"Beta-adrenergic receptor antagonists have been shown to reduce the production of melatonin via specific inhibition of beta-1 adrenergic receptors. Nighttime administration of beta- adrenergic receptor antagonists may reduce the efficacy of tasimelteon." Weisbruch Decl. Ex. 2 (Teva's Label) at 3; Weisbruch Decl. Ex. 4 (Apotex's Label) at 4. Teva's description of the reduction of efficacy of tasimelteon will induce at least some physicians to instruct their patients to stop taking beta blockers. Combs Decl. ¶¶ 48–54.
Administering to the patient 20 mg of tasimelteon once daily about one-half hour to about one-and-one-half hours before the target bedtime	"The recommended dosage of tasimelteon capsules in adults is 20 mg one hour before bedtime . . . ." Weisbruch Decl. Ex. 2 (Teva's Label) at 2; Weisbruch Decl. Ex. 4 (Apotex's Label) at 3.
'129 Claim 2	**Teva Label**
The improvement of claim 1, wherein the beta-adrenergic receptor antagonist is selected from a group consisting of: alprenolol, alternolol, carvedilol, metoprolol, and propranolol.	"7.3 Beta-Adrenergic Receptor Antagonists (e.g., acebutolol, metoprolol)." Weisbruch Decl. Ex. 2 (Teva's Label) at 3; Weisbruch Decl. Ex. 4 (Apotex's Label) at 4.
'129 Claim 3	**Teva Label**
The improvement of claim 2, wherein the patient is suffering from Non-24-Hour Sleep-Wake Disorder	"Tasimelteon capsules are indicated for the treatment of Non-24 in adults." Weisbruch Decl. Ex. 2 (Teva's Label) at 2; Weisbruch Decl. Ex. 4 (Apotex's Label) at 3.

Claim 1 is directed to a method of administering tasimelteon to a patient by determining whether the patient is being treated with a beta-adrenergic receptor antagonist (beta blockers), and if the patient is on beta blockers, the patient should be instructed to stop taking beta blockers and then take tasimelteon once a day before bedtime. *See* TVC Ex. A at 38:41-56; AVC Ex. A at 38:41-56. Teva's and Apotex's labels induce doctors to infringe the claims of the '129 patent because they "encourage" discontinuation of beta-blockers by instructing on the reduced efficacy of tasimelteon when co-administered with tasimelteon. *See* Weisbruch Decl. Ex. 2 (Teva's Label) at 3; Ex. 4 (Apotex's Label) at 4; Combs Decl. ¶¶ 63–67. A physician could understand Teva's and Apotex's labels to counsel asking potential drug recipients whether they are on beta blockers or not, and if so, to instruct the patient to stop before taking tasimelteon. *See* Combs Decl. ¶ 54. Teva's and Apotex's labels further induce infringement of dependent claims 2 and 3 by encouraging the infringing methods both with respect to metoprolol and for Non-24 patients. *See* Table 1, *supra*.

Infringement has routinely been found in circumstances like this, where the prescribing information would induce infringement. *See, e.g.*, *Eli Lilly*, 845 F.3d at 1369 ("[E]vidence that the product labeling that Defendants seek would inevitably lead some physicians to infringe establishes the requisite intent for inducement."); *Sanofi*, 875 F.3d at 645 (affirming induced infringement where the label "directs

medical providers to information identifying the desired benefit for only patients with the patent-claimed risk factors" and "considerable testimony that this label encourages ... administration of the drug to those patients"); *AstraZeneca*, 633 F.3d at 1060 (affirming finding of induced infringement where "despite being aware of the infringement problem presented by the proposed label, Apotex nonetheless proceeded with its plans to distribute its generic drug product").

b. The reasons Teva and Apotex provided in their Paragraph IV detailed statements for why each does not infringe are unpersuasive. Teva contended that (1) "there is no direct infringement, which is required for induced or contributory infringement"; (2) "there is no instruction or direction in Teva's labeling to perform the steps of the method claims of the '129 patent" because "[t]here is no instruction in Teva's labeling to determine if a patient is treated with a beta-adrenergic receptor antagonist" and (3) there is no "instruction in Teva's labeling to inform a patient to cease treatment with a beta-adrenergic receptor antagonist." Weisbruch Decl. Ex. 1 (Teva's Paragraph IV Certification) app. at 7. Each contention is fundamentally wrong.

Teva is wrong to claim that "there is no direct infringement" of the '129 claims. While Teva may not itself administer tasimelteon to patients in violation of the '129 patent, others *will* do so based on the encouragement that Teva's infringing label provides. Therefore, if Teva's ANDA product is permitted to come to market,

direct infringement—induced by Teva's unlawful acts—will take place in the marketplace to Vanda's detriment. Combs Decl. ¶¶ 59-72.

Teva's second and third points are also incorrect. Teva's argument casually brushes over the fact that its own label—which Teva submitted to FDA when it requested approval of its tasimelteon ANDA product and which is required to be substantially similar to Vanda's Hetlioz® label—encourages tasimelteon not to be administered concurrently with beta blockers:

> Beta-adrenergic receptor antagonists have been shown to reduce the production of melatonin via specific inhibition of beta-1 adrenergic receptors. Nighttime administration of beta- adrenergic receptor antagonists may reduce the efficacy of tasimelteon.

Weisbruch Decl. Ex. 2 (Teva's Label) at 3.

Physicians in the field would understand Teva's label to advise against co-administration of tasimelteon and beta blockers. Combs Decl. ¶¶ 65-66. As physicians rely on labels when prescribing drugs to patients and want patients to have the most efficacious treatment, they would thus understand Teva's label to counsel asking potential drug recipients whether they are on beta blockers or not, and if so, direct that the patient not take beta blockers and tasimelteon simultaneously. *See* Combs Decl. ¶¶ 53-54. Indeed, armed with the knowledge of the negative interaction between beta blockers and tasimelteon, at least some doctors would substitute a different medication that treats the same condition for the beta blocker. *See* Combs Decl. ¶¶ 55-58. These physicians would directly infringe by

merely following the language of Teva's label. Teva's label will therefore induce infringement.

For its part, Apotex likewise contended that (1) the label "does not encourage, recommend, or promote health care providers to determine whether a patient is taking a beta-adrenergic receptor antagonist"; and (2) "health care providers … would be free to exercise their own discretion to determine whether Apotex's ANDA Product could be co-administered with a beta-adrenergic receptor antagonist." Weisbruch Decl. Ex. 3 (Apotex's Paragraph IV Certification) at A-26. Again, though, some physicians would understand Apotex's label to counsel asking potential drug recipients whether they are on beta blockers or not, and if so, directing that the patient not take beta blockers and tasimelteon simultaneously. *See* Combs Decl. ¶¶ 52-54.

2. Vanda will likely prove infringement under Section 271(e) because the generics' ANDA submissions infringe at least one claim of the '129 patent.

This Court need not look solely to the future to determine whether Teva and Apotex will infringe. Rather, as explained above, Teva and Apotex submitted an ANDA—now approved—to market a generic version of Hetlioz®. Because Teva's application sought approval "for a drug[,] … the use of which is claimed in" the '129 patent, it has already infringed the '129 patent by filing its ANDA for the same

reasons that it will induce infringement should it be allowed to launch its product. 35 U.S.C. § 271(e)(2)(A).

"An infringement inquiry pursuant to 35 U.S.C. § 271(e)(2)(A) 'is focused on a comparison of the asserted patent [claims] against the product that is likely to be sold following ANDA approval.'" *Vanda Pharms.*, 887 F.3d at 1125 (alteration in original) (quoting *Alcon Rsch. Ltd. v. Barr Labs., Inc.*, 745 F.3d 1180, 1186 (Fed. Cir. 2014)). A plaintiff must show "(1) direct infringement, *i.e.*, if the defendant's drug was 'put on the market, it would infringe the relevant patent'; and (2) 'that [defendant] possessed the specific intent to encourage another's infringement.'" *Genentech, Inc. v. Sandoz Inc.*, 2022 WL 17839055, at *6 (Fed. Cir. Dec. 22, 2022) (alteration in original) (quoting *Vanda Pharms.*, 887 F.3d at 1129-1130 (Fed. Cir. 2018)).

In the context of method of use claims (like those in the '129 patent), ANDA applicants infringe a method of use where the proposed label "would inevitably lead some physicians to infringe." *Eli Lilly*, 845 F.3d at 1369; *see also Sanofi*, 875 F.3d at 645; *AstraZeneca*, 633 F.3d at 1060-61. Because of the nature of Section 271(e)(2)(A) infringement, "a patentee does not need to prove an actual past instance of direct infringement by a physician to establish infringement under 35 U.S.C. § 271(e)(2)(A)" nor must it prove, for method patents, "that prior use of the NDA-approved drug satisfies the limitations of the asserted claims." *Vanda Pharms.*, 887

F.3d at 1129-30. Rather, it suffices to "prove the predicate direct infringement [for induced infringement] by showing that if the proposed ANDA product were marketed, it would infringe." *Id.* at 1130.

For the same reasons as explained in Section I.A.1, Vanda is likely to prove infringement under 35 U.S.C. § 271(e)(2) by Teva's and Apotex's submission of ANDAs with prescribing information that will induce physicians to infringe the claim limitations of the '129 patent.

3. Teva and Apotex cannot raise a substantial question concerning the validity of the '129 patent.

Vanda is further likely to succeed on the merits because Teva and Apotex cannot raise a substantial question concerning the validity of the '129 patent.

The '129 patent is a duly issued U.S. patent, and it is "presumed valid." 35 U.S.C. § 282(a). Vanda has thus satisfied its burden at this stage to establish eligibility for the requested interim relief. *Purdue Pharma L.P. v. Boehringer Ingelheim GMBH*, 237 F.3d 1359, 1365 (Fed. Cir. 2001). This presumption of validity is bolstered by the prosecution history, which reflects that the Patent Office identified no substantive problems—issuing not a single rejection—before allowing the claims (Weisbruch Decl. Ex. 9 ('129 Notice of Allowability) at 2–3), even though Vanda submitted more than 200 references for the examiner's consideration (*see* Weisbruch Decl. Ex. 10 (Pros. History IDS)).

Beyond that, Teva and Apotex are not "likely to succeed in proving invalidity

or unenforceability of the asserted patents" (*Abbott Labs. v. Andrx Pharms., Inc.*, 473 F.3d 1196, 1201 (Fed. Cir. 2007)) for at least two reasons.

First, neither Teva nor Apotex proffered a single reasoned argument in the detailed statement accompanying their Paragraph IV letters contending that the '129 patent is invalid. Weisbruch Decl. Ex. 1 (Teva's Paragraph IV Certification) app. at 7–8; Ex. 3 (Apotex's Paragraph IV Certification) at A25-26. Teva and Apotex did not do so despite their obligations to "include a detailed statement of the factual and legal basis of the opinion of the applicant that the patent is invalid or will not be infringed" (21 U.S.C. § 355(b)(3)(D)(ii)). Teva's and Apotex's own notices to Vanda confirm that neither is "likely to succeed in proving invalidity or unenforceability of the asserted patents." *Abbott Labs.*, 473 F.3d at 1201; *see also Canon Computer Sys., Inc. v. Nu-Kote Int'l, Inc.*, 134 F.3d 1085, 1088 (Fed. Cir. 1998). The failure to include a full argument when they had the opportunity and obligation to do so is proof that Teva and Apotex will not be able to establish here what they did not have at the time of their certifications: a likelihood of success in invalidating the '129 patent.[5]

[5] Rather than develop any argument, Teva offered, in passing, a single citation, suggesting that this renders the claims obvious. Weisbruch Decl. Ex. 1 (Teva's Paragraph IV Certification) app. at 8 (citing Scheer FA et al., *Decreased sleep in heart failure: are medications to blame?*, 167 Archives of Internal Medicine 1098-1099 (2007) ("Scheer")). Scheer, mere editor's correspondence, actually shows the opposite. The '129 patent covers treating a patient diagnosed with Non-24 with

Second, as Vanda will further prove (if necessary), Teva and Apotex are not "likely to succeed" in providing clear and convincing evidence that any claim of the '129 patent is invalid even were they to try. Notably, years before Hetlioz® was FDA approved, Vanda's own research invented a method of treatment that was sensitive to the interaction between tasimelteon and beta blockers. The resulting methods of administration were not just novel; they embody numerous objective indicia of nonobviousness.

Objective indicia can "be the most probative and cogent evidence of nonobviousness in the record" (*Ortho-McNeil Pharm., Inc. v. Mylan Lab'ys, Inc.*, 520 F.3d 1358, 1365 (Fed. Cir. 2008)) and are "not merely 'icing on the cake'" or an "afterthought" (*Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1380 (Fed. Cir. 1986); *Leo Pharm. Prods., Ltd. v. Rea*, 726 F.3d 1346, 1357 (Fed. Cir. 2013)).

One such indicia is unexpected results. Here, the negative interaction of beta

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tasimelteon *without* a beta blocker. Yet Scheer proposes supplementing a heart failure patient's beta blockers (which may cause reduced sleep) *with* exogenous nighttime melatonin to counteract the beta blocker's effects. This is the opposite of the claimed invention in multiple ways—it says nothing about patients with Non-24, it does not address tasimelteon, and, if anything, it would suggest that beta blockers should be used with therapies that supplement melatonin. A data-backed comment written by responding doctors criticized Scheer's conclusions about whether beta blockers induce sleep loss and the relationship between beta blockers and sleep loss. Perhaps of most interest, the reply comment specifically explained that physicians should not be deterred from prescribing beta blockers based on any sleep loss—again, the opposite of the patented treatment methods.

blockers and tasimelteon would not have been expected in light of literature both before and after the priority date of the '129 patent suggesting that beta blockers could be useful in the treatment of circadian rhythm disorders. *E.g.*, Weisbruch Decl. Ex. 11 (Leersnyder 2001) at 586; Weisbruch Decl. Ex. 12 (Gehrman 2021) at 2121-23 (discussing the use of a combination of a beta blocker and the administration of exogenous melatonin in treating a patient with a circadian rhythm disorder).

The prior art thus taught away from the claimed invention. *See Allergan, Inc. v. Sandoz Inc.*, 796 F.3d 1293, 1305 (Fed. Cir. 2015) ("A reference may be said to teach away when a person of ordinary skill, upon reading the reference ... would be led in a direction divergent from the path that was taken by the applicant." (quoting *In re Gurley*, 27 F.3d 551, 553 (Fed. Cir. 1994)). This is powerful evidence of non-obviousness.

Because Teva and Apotex have not (and will not be able to) raise a substantial question as to validity, Vanda has established its likelihood of success on the merits, warranting a grant of a temporary restraining order.

B. Vanda will suffer substantial irreparable harm unless Teva and Apotex are immediately enjoined to preserve the status quo.

Absent immediate, temporary relief, Vanda will suffer substantial, irreparable harm. Several points establish the immediate and irreparable nature of the harm.

First, there can be no reasonable dispute that Teva and Apotex are ready and able to launch their Hetlioz® copycats immediately. They recently told the Federal

Circuit as much. Teva extolled its "ability to immediately launch a generic tasimelteon product" and its "position[ing] for an immediate product launch," as well as supposed December sales that the Federal Circuit's temporary injunction was prohibiting. *See* Teva Pharms. USA, Inc.'s Non-Confidential Emergency Mot. for Review, Reconsideration, or Modification of Temporary Injunction at 2, 18, *Vanda Pharms. Inc. v. Teva Pharms. USA, Inc.*, No. 23-1247 (Fed. Cir. Dec. 19, 2022), ECF No. 9. Apotex has similarly represented that it is prepared to launch. *See* Apotex's Opp. to Appellee Teva's Emergency Mot. at 1, *Vanda Pharms. Inc. v. Teva Pharms. USA, Inc.*, No. 23-1247 (Fed. Cir. Dec. 21, 2022), ECF No. 16; Appellees' Response in Opp. to Appellant's Rule 8 Motion for an Injunction Pending Appeal at 14, *Vanda Pharms. Inc. v. Teva Pharms. USA, Inc.*, No. 23-1247 (Fed. Cir. Dec. 23, 2022), ECF No. 25. Absent an order from this Court, Teva and Apotex will launch.[6]

Second, the magnitude of harm to Vanda is extraordinary: Vanda has two products in the marketplace, Fanapt® and Hetlioz®. Hetlioz® makes up about 65% of Vanda's revenue. Moran Decl. ¶ 7. While Vanda is fortunate to have on hand material cash and marketable securities, if it is deprived of a substantial portion of its largest revenue generator, Vanda's CFO has attested that it "is uncertain whether the cash provided by Vanda's operating activities, together with the existing funds,

[6] Indeed, both Teva and Apotex have received FDA final approval and the ability to immediately launch a generic tasimelteon product. Weisbruch Decl. Ex. 7 (Teva's ANDA Final Approval); Ex. 8 (Apotex's ANDA Final Approval).

will be sufficient to meet Vanda's long-term operating needs." *Id*. ¶ 10. Further, Mr. Moran explains that the loss of revenue is likely to be so severe that it would "lead to a decrease in Vanda's ability to continue operations in their current form." *Id*. ¶ 14. The launch of tasimelteon generics thus could pose existential threats to Vanda—a factor that overwhelmingly establishes irreparable injury. *In re Revel AC, Inc.*, 802 F.3d 558, 572 (3d Cir. 2015) (irreparable injury is shown when "the potential economic loss is so great as to threaten the existence of the movant's business"); *Eisai Co., Ltd v. Teva Pharms. USA, Inc.*, 2008 WL 1722098, at *11 (D.N.J. Mar. 28, 2008) (finding irreparable harm where brand drug constituted "70% of [patentee's] U.S. subsidiary's profits," and company "organized its business plans in reliance on patent exclusivity").

Third, a generic entry would irreparably and detrimentally alter the market for Hetlioz®. *See Presidio Components, Inc. v. American Tech. Ceramics Corp.*, 702 F.3d 1351, 1363 (Fed. Cir. 2012) ("Direct competition in the same market is certainly one factor suggesting strongly the potential for irreparable harm without enforcement of the right to exclude.").

Through enormous hard work and direct services, Vanda has reduced the attrition rate of patients prescribed tasimelteon, by assisting patients with insurance coverage issues and through direct outreach and education programs. Moran Decl. ¶ 22; Grabowski Decl. ¶ 64. Right now, patient attrition rates are generally in the

single-digits—*because of Vanda's services to those prescribed Hetlioz*®—but patients prescribed a generic (or whose insurer or pharmacist substitutes a Hetlioz® prescription for a generic) will not have those services and thus the attrition rate will likely rise markedly. Moran Decl. ¶ 14; Grabowski Decl. ¶ 64. The result is a loss for the entire tasimelteon market that cannot later be recovered, and for which Vanda cannot later be made whole.

Further, if generics enter the market only later to be removed from it, the end result is that Hetlioz® may be dropped from drug formularies, making it far more difficult for patients to access the medication and enormously decreasing the market. Grabowski Decl. ¶¶ 25, 34, 38, 39. This injury cannot be later fixed. *See Sanofi-Synthelabo v. Apotex, Inc*., 470 F.3d 1368, 1382 (Fed. Cir. 2006) ("[T]he availability of a generic product encourages third party payors to place Plavix® on a less favorable tier, thereby requiring consumers to pay a higher co-pay, and perhaps deterring them from purchasing Plavix®."); *see also Glaxo Group Ltd. v. Apotex, Inc.*, 64 F. App'x 751, 756 (Fed. Cir. 2003) (affirming finding that a drug patentee demonstrated irreparable harm by showing that "generic entry, even if it is not the first generic competition, would affect not only price and profit but also cause a significant loss in market share").

Fourth, Vanda would irreparably lose good will—and the price of Hetlioz® would be permanently eroded. Grabowski Decl. ¶¶ 33, 37, 40. Indeed, Vanda will

suffer irreparable harm to its goodwill and reputation as physicians, pharmacists, and consumers become accustomed to using Teva's infringing products as a substitute for Hetlioz. Courts have consistently found that these factors support a finding of irreparable injury. *See Celsis In Vitro, Inc., v. Cellzdirect, Inc.*, 664 F.3d 922, 930 (Fed. Cir. 2012); *Abbott Labs. v. Sandoz, Inc.*, 544 F.3d 1341, 1362 (Fed. Cir. 2008) (affirming conclusion that price erosion constituted irreparable harm); *Sanofi-Synthelabo*, 470 F.3d at 1381; *Purdue Pharma L.P. v. Boehringer Ingelheim GMBH*, 237 F.3d 1359, 1368 (Fed. Cir. 2001) (likelihood of price erosion and loss of market position are evidence of irreparable harm); *Bio-Tech. Gen. Corp. v. Genentech, Inc.*, 80 F.3d 1553, 1566 (Fed. Cir. 1996) (loss of revenue, goodwill, and reduced research and development activities constitute irreparable harm).

Fifth, and critically, the net effect of generic competition would be massive injury to Vanda's ongoing research and development efforts—both for new applications for use of Hetlioz® as well as other innovative drugs in Vanda's pipeline. For the first 9 months of 2022, "Vanda reinvested approximately 90% of its total revenue into research and development and company operations." Moran Decl. ¶ 8. Right now, Vanda is attempting to develop new indications for Hetlioz®, including jet lag disorder, insomnia, delayed sleep phase disorder ("DSPD"), and sleep disturbances for patients with autism spectrum disorder ("ASD"). *Id.* ¶ 9. But if generics launch, Vanda will lose both the financial ability to fund these activities

as well as the economic incentive to do so. *Id.* ¶¶ 14-18.

Additionally, Vanda would lose funds needed for its research and development into several other promising therapeutics, including products to address gastroparesis, secretory diarrhea disorders including cholera, and acute performance anxiety. Moran Decl. ¶¶ 9, 18. The harms to this ongoing research are irreparable. *See Eisai Co., Ltd*, 2008 WL 1722098, at *11 (identifying loss of research and development investment resulting from lost product sales as irreparable harm); *Bio-Tech.*, 80 F.3d at 1566 (reduced research and development activities constitute irreparable harm).

C. The balance of hardships favors a temporary restraining order

The balance of hardships—disastrous irreparable consequences for Vanda against loss of compensable money for generic-giants Teva and Apotex—favors issuing the requested temporary restraining order. To assess the balance, "the district court must balance the harm that will occur to the moving party from the denial of the [] injunction with the harm that the non-moving party will incur if the injunction is granted." *Hybritech Inc. v. Abbott Labs.*, 849 F.2d 1446, 1457 (Fed. Cir. 1988). The balance tips decidedly in favor of the temporary restraining order.

First, on Vanda's side of the scale, there is severe and immediate irreparable harm. Vanda will suffer irreparable losses of company-essential revenues, market size, market share, formulary placements, good will, plus price erosion and hindered

or curtailed research and development and operations—all irreparable harms that follow from the infringement of Vanda's rights in the '129 patent.

By not enjoining Teva and Apotex from infringing, the value of Vanda's exclusionary rights in the '129 patent will be all but destroyed. "In instances where the patent owner will suffer diminution in the value of its patent, the balance of hardships weighs in the owner's favor." *Everett Labs., Inc. v. Breckenridge Pharm., Inc.*, 573 F. Supp. 2d 855, 870 (D.N.J. 2008).

Second, on Teva's and Apotex's side of the scale, there is no irreparable harm whatsoever. All that Teva and Apotex stand to lose is money. And—from the vantage of these massive generic manufacturers—it is a meager amount of money at that, considering how small the market is for treating the rare condition of Non-24. *See* Grabowski Decl. ¶ 541. A temporary restraining order simply prevents generics from further exploitation and infringement of Vanda's '129 patent, a self-inflicted injury when considering the weakness of their Paragraph IV certifications, asserting in only conclusory fashion that their generic products would not infringe the '129 patent. *See Feist Publications, Inc. v. Rural Tel. Serv. Co.*, 499 U.S. 340, 379 (1991) (holding that the potential harm faced by respondents is self-inflicted, and damage to plaintiff from infringement is far worse); *see Pappan Enters., Inc. v. Hardees Food Sys., Inc.*, 143 F.3d 800, 806 (3d Cir. 1998) ("The self-inflicted nature of any harm suffered by [the party opposing the injunction] also weighs in favor of granting

preliminary injunctive relief.").

Comparing Vanda's irreparable harm to the utter absence of any for Teva and Apotex clearly weighs in Vanda's favor. And these harms are particularly mismatched here. Teva has nearly 60 times the revenue of Vanda and sells hundreds of generic drugs, compared to Vanda's two FDA-approved drugs. Apotex similarly has 12 times Vanda's revenue, with a product offering reaching the hundreds. This significant disparity in hardships suffered weighs heavily in favor of granting Vanda relief. Grabowski Decl. ¶ 54; *see Glaxo Group*, 64 F. App'x at 756 (affirming finding that "without the preliminary injunction, [the branded company] would lose the value of its patent while [the generic company] would only lose the ability to go on to the market and begin earning profits earlier").

Further, through a bond, Vanda will guarantee that any harm Teva or Apotex may suffer through an injunction later deemed improper are fully remedied. Teva and Apotex thus cannot suffer injury.

In sum, the balance of hardships tips decidedly in favor of Vanda.

D. The public interest favors a temporary restraining order

Issuance of the temporary restraining order would uphold the effectiveness of the U.S. patent system and encourage innovation, thereby serving the public interest. Indeed, there is a "significant 'public interest in encouraging investment in drug development and protecting the exclusionary rights conveyed in valid

pharmaceutical patents.'" *Sanofi-Synthelabo*, 470 F.3d at 1384 (citation omitted); *see also AstraZeneca LP v. Apotex, Inc.*, 623 F. Supp. 2d 579, 614 (D.N.J.), *supplemented*, 623 F. Supp. 2d 615 (D.N.J. 2009), *aff'd*, 633 F.3d 1042 (Fed. Cir. 2010), *and aff'd*, 633 F.3d 1042 (Fed. Cir. 2010). Here, this usual public interest is particularly strong in Vanda's case as a company that specializes in identifying older, abandoned molecules, acquiring them from companies in whose hands they failed, identifying uses for those compounds, and securing FDA approval. Taking abandoned drugs and successfully developing them for unmet medical needs is surely in the public interest.

Moreover, any public interest the other way should not outweigh the strong interest in protecting Vanda's patent rights during the brief amount of time necessary for the Court to decide a preliminary injunction. *Sanofi-Synthelabo*, 470 F.3d at 1383. After all, "[s]elling a lower priced product does not justify infringing a patent." *Pfizer, Inc. v. Teva Pharms. USA, Inc*, 429 F.3d 1364, 1382 (Fed. Cir. 2005) (quoting *Payless Shoesource, Inc. v. Reebok Int'l Ltd.*, 998 F.2d 985, 991 (Fed. Cir. 1993)). "[T]he statutory framework" under Hatch-Waxman does not "eliminat[e] the exclusionary rights conveyed by pharmaceutical patents," nor does it "encourage or excuse infringement of valid pharmaceutical patents." *Id.* at 1382-1383 (affirming preliminary injunction against generic).

The public interest thus favors the status quo that a temporary restraining order

will preserve.

II. The pending litigation in the Federal Circuit does not counsel against injunctive relief.

Vanda wishes to be clear: Vanda is seeking this emergency relief early in the morning today, December 29, 2022, because yesterday afternoon, on December 28, the Federal Circuit lifted an injunction it previously had in place barring Teva and Apotex from launching. That action by the Federal Circuit does not counsel against the relief requested here.

As we said above, Vanda previously sued Teva and Apotex on other patents, which resulted in a recent final judgment favorable to the generics. *See* Final Judgment, *Vanda Pharms. Inc. v. Teva Pharms. USA, Inc.*, No. 18-cv-651 (D. Del. Dec. 13, 2022), ECF No. 338. That district court ordered on consent a short-term "status quo" order, precluding Teva and Apotex from launching until such time as the Federal Circuit could resolve a request for injunctive relief. *See id.* at 3. The Federal Circuit then issued an emergency order further barring Teva and Apotex from launching until it could resolve the merits of Vanda's request for a Rule 8 injunction—which sought an injunction pending the appeal. *See* Order on Motion for Injunction Pending Appeal, *Vanda Pharms. Inc. v. Teva Pharms. USA, Inc.*, No. 23-1247 (Fed. Cir. Dec. 16, 2022), ECF No. 6. Notably, the Federal Circuit issued relief directly analogous to that which Vanda requests here—an order barring a launch for a brief period of time *until* the court may address the request for a longer

term stay.

To be sure, the Federal Circuit denied a longer-term injunction pending appeal. To secure that relief, Vanda had to demonstrate a likelihood that the Federal Circuit would overturn an existing adverse decision issued by the district. This case stands on very different footing, however, because there has not been any litigation yet regarding the '129 patent, much less a decision adverse to Vanda. And, again, this patent issued *during* the earlier trial and was thus obviously not a patent that could have been litigated in that earlier proceeding. Indeed, Apotex did not notify Vanda of its Paragraph IV Certification regarding the '129 patent until June 15, 2022, while Teva did not until September 12, 2022.

In sum, the Federal Circuit's resolution of Vanda's Rule 8 motion seeking long term relief—where the central issue is whether Vanda is likely to overturn an unfavorable decision on appeal—says little as to whether this Court should grant short term relief to preserve its ability to rule on a forthcoming motion for a preliminary injunction regarding an entirely different patent.

III. Vanda will post a bond.

Should this Court issue a temporary restraining order, Vanda is willing to post an appropriate bond as the Court directs. As a preliminary matter, Teva and Apotex jointly told the Federal Circuit that, were they enjoined from launching their generic products, any bond should collectively be "$50 million for a 12-month injunction,"

or $4.16 million per month collectively. *See* Appellees' Response in Opp. to Appellant's Rule 8 Motion for an Injunction Pending Appeal, *Vanda Pharms. Inc. v. Teva Pharms. USA, Inc.*, No. 23-1247 (Fed. Cir. Dec. 23, 2022), ECF No. 25.

While Vanda has deep reservations about Teva and Apotex's calculations, Vanda is willing to accept it as a starting point for present purposes, so as to minimize the issues in dispute. Two adjustments, however, are necessary.

First, it appears that Teva and Apotex were using a market size of $165 million per year, which was the total market size for 2021. But, as Mr. Moran explains (Moran Decl. ¶¶ 23), this base needs to be adjusted because sales appear to have decreased in 2022 to a total of $160 million, and only $149 million of that base amount reflects sales of Hetlioz® in the United States. This is a reduction of $16 million in base, or 9.7%.

Second, defendants do not account for patient attrition or acquisition. Vanda has experienced attrition rates at the mid-single digits per month but only because of its extensive patient support and education, marketing, and reimbursement services. Moran Decl. ¶¶ 14, 20, 22. Vanda's services also assist patients in accessing Hetlioz®, leading to increased patient acquisition to offset any attrition. Moran Decl. ¶ 22. Without these additional services that Vanda will reduce were generics to enter the market and that generic patients will not have at all, the patients actually served is likely to contract by more than 30%. Moran Decl. ¶ 22.

Taken together, Vanda submits that the bond amount requested by Teva and Apotex should be reduced, at minimum, by 39.7%, resulting in an annual bond amount of $30,150,000. This is $2,512,500 on a monthly basis, which Vanda submits should be divided evenly as $1,256,250 per defendant per month.

Vanda thus requests that the Court order a running bond of $1,256,250 per month as to Teva and Apotex each. Whatever bond the Court may order—be it Vanda's proposal, the request of Teva and Apotex for a total of $4.16 million per month, or some number in between—Vanda requests that it be ordered to post bond for a one-month period no later than 5pm on January 4, 2023. If additional time is needed for the Court to resolve Vanda's forthcoming motion for a preliminary injunction, Vanda requests that it be obligated to post an additional month of bond by the 4th of each month (or the immediately following business day).

CONCLUSION

The Court should grant a temporary restraining order to preserve the status quo, precluding Teva and Apotex from launching a generic, until such time as this Court may adjudicate a preliminary injunction motion. The Court should further obligate Vanda to post bond in an amount that the Court determines is just and reasonable.

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Newark, New Jersey

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